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| ACUTE INHALATION IN MALE RATS | | |
| **Chemical Category** | | |
| METHYLENE-BIS-(4-PHENYLISOCYANATE) | | |

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine

HASKELL LABORATORY REPORT NO. 62-65

Material Tested: Methylene-bis-(4-Phenylisocyanate); MDI; Hylene M®

## ACUTE INHALATION

Method: A weighed amount of material was placed in a 500 cc 3-necked flask. It was heated to, and maintained at, the required temperature with a heating mantle. A dry air stream (2 liters/min.) through the flask carried the vapors to an 8-liter bell jar containing four CbR-CD male rats.

Results:

| Temp. (°C) | Initial Wt. Material (gm) | Wt. Loss (gm) | Nominal Concentration mg/liter | Nominal Concentration ppm | Durat' Expo (h | Mortality Ratio | Fate |
|---|---|---|---|---|---|---|---|
| 300* (336) | 20.53 | 5.45 | 11 | 1075 | 4 | 2/4 | One died during exposure (1 hr. 22 min.). One died one day after exposure. Two killed 16 days after exposure. |
| 300* (320) | 20.38 | 5.81 | 12 | 1175 | 4 | 3/4 | Three died: 2 3/4 and 3 3/4 hrs. during exposure and 23 min. after exposure. |
| 200 | 19.77 | 4.71 | 10 | 978 | 4 | 0/4 | Killed 17 days after exposure. |

Clinical Observations During Life: The approximate lethal temperature of H-3254 is 300°C for four hours. At lethal temperatures (300-336°C), rats showed eye irritation, labored breathing and gasping, and were pale and their fur stained yellow during exposure. Rats surviving exposure had weight losses and ruffled fur for two days; one rat was weak and had respiratory impairment for about five days. Slightly scaly ears were observed in some of these rats eight days after exposure, but all appeared normal at sacrifice. The material, when heated to temperatures of 300°C or higher, decomposed and was hard and charred by the end of exposure.

* Temperature overshot to 336°C for 1/2 hour and 320°C for 5 minutes. This was most likely caused by heat released by decomposition of the material.

Rats exposed to the material at the sublethal temperature (200°C) had rapid and deep respiration, eye irritation and stained fur during exposure, and weight losses for 1-2 days after exposure. Scaly ears were observed in these rats from the 7-9th day after exposure, but all appeared normal thereafter. At this temperature, the material turned dark and liquified and remained in this state even when cool.

Pathology: The rats succumbing at 300°C showed pulmonary congestion and edema. The survivors at this temperature showed no histologic effects when sacrificed 14-16 days after exposure. No effects attributable to the compound were observed in the tissues of rats exposed to MDI at 200°C.

Discussion: MDI was lethal to 2/4 rats after a four-hour exposure to a nominal 11 mg/liter of material from MDI heated at 300°C. This is in comparison to TDI which was lethal to 2/2 rats after a 6 1/2-hour exposure to a nominal 4 mg/liter from toluene-2,4-diisocyanate (TDI) heated at 100°C.

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## PRIMARY SKIN IRRITATION

Methylene-bis-(4-phenylisocyanate) was applied in solution at three concentrations of active ingredient. It was applied in a 1:1 acetone:dioxane solvent system containing 13% guinea pig fat and was applied to the shaved, intact, skin of male albino guinea pigs. It was more irritating to the skin of guinea pigs than was toluene-2,4-diisocyanate.

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Summary: MDI has an Approximate Lethal Concentration (ALC) by inhalation of 11 mg/liter. This is in comparison to TDI which has an ALC of 4 mg/liter. Both are temporary respiratory irritants and also cause lacrimation. MDI is more irritating to the skin than TDI. MDI should be handled with care, and only in well ventilated areas. The ACGIH has recommended (1965) a tentative Threshold Limit Value of 0.02 ppm for MDI.

Recommendations: If extensive use of MDI is being considered, it is recommended that skin sensitization and subacute inhalation tests be carried out. As other organic isocyanates, MDI should be considered a skin sensitizer.

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Date: May 12, 1965

## CERTIFICATE OF AUTHENTICITY

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